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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,649	10/07/2003	Robert A. Holton	FSUM 10442.19	5089

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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/680,649	HOLTON, ROBERT A.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/29/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Claims 1-17 are presented for prosecution on the merits.

Information Disclosure Statement

Applicant's Information Disclosure Statement received Dec. 29, 2003 has been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. Applicant is respectfully requested to update the status of parent application 09/776,426 to include the corresponding patent number 6,638,973.

Claim Rejections—35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a limited number of cancers, does not reasonably provide enablement for the broad number of cancers embraced by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The claims are drawn to a method of treating a neoplastic cancer in a patient in need thereof by administering to the patient an effective amount of a taxane compound.

(2) The state of the prior art

With respect to the term "neoplastic cancer", this a broad term which encompasses numerous forms of neoplastic diseases or cancers, each involving different types of tissues and organs. As recognized in the art, many different

antineoplastic drugs are used to treat a variety of cancers, but there is no one drug which is capable of treating all cancers in general. Please see Goodman & Gilman's, Section X, Table X-1, pages 1227-1229. Furthermore, Goodman & Gilman's does not disclose that the taxane compounds paclitaxel and docetaxel have clinical activity or significant response rates against all cancers. Instead, these compounds have shown activity against ovarian cancer, and "have promising activity" against breast, head, neck, esophageal and lung cancers. Please see pages 1260-1261.

(3) The relative skill of those in the art

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical and chemical art is high.

(5) The breadth of the claims

The claims are very broad and encompass treatment of numerous types of cancers.

(6) The amount of direction or guidance presented

Applicant's specification does not enable one of ordinary skill in the art to use the claimed taxane compounds in the treatment of the numerous types of cancers covered by the term "neoplastic cancer." Other than the specific examples of cancers discussed in the Background of The Invention, Applicant has not set forth a representative number of examples of cancers against which the claimed compounds would be active.

(7) The presence or absence of working examples

The only working examples in the specification appear to involve the in vitro activity of the taxane compounds in an assay using HCT116 colorectal cell lines. There are no other working examples involving the use of the claimed compounds and their activity against of other cells lines.

(8) The quantity of experimentation necessary

Since (1) the art recognizes that no one compound is capable of treating the numerous diseases encompassed by the term "neoplastic cancer"; (2) the art acknowledges clinical activity against ovarian and potential activity against other limited types of cancers; (3) since the claims are very broad and require the treatment of numerous types of cancers, and (4) since Applicant's specification does not provide guidance or a representative number of working examples of neoplastic cancers which can be treated with the taxane compounds of the invention, one of ordinary skill in the art would be burdened with undue experimentation to determine which of the many diseases embraced by Applicant's claims would be treated by the claimed compounds.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-2, 4-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 1 recites the limitation "ethanol" in line 9. There is insufficient antecedent basis for this limitation in the claim.

4. Claims 7-9, 12-17 recite the limitation "the HCT116 cell line" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections—35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable Broder et al., 6,395,770 B1 and McChesney-Harris, US 2001/0029264 A1 in view of Goodman & Gilman's, The Pharmacological Basis of Therapeutics, Ninth Edition.

Broder et al. disclose a method of treating human patients suffering from taxane-responsive diseases. Specifically, the method involves a dual dosing regimen, which comprises orally administering effective amounts of a composition containing a taxane compound such as paclitaxel. The composition may be in liquid form and comprises the taxane in a CREMOPHOR EL™vehicle, which consists of polyethoxylated castor oil and alcohol (please see specification page 1, lines 30-34). Additional excipients present in

the oral composition are dextrose and water as well as sweetening agents. Please see the abstract; col. 5, lines 58-61; col. 6, lines 58-67; col. 10, lines 16-21; col. 12, lines 12-25; Example 3, line 66 to col. 15, line 2.

McChesney-Harris discloses a method of treating a taxane-responsive disease by orally administering a composition containing a taxane, polyethoxylated castor oil, ethanol, water as well as additional surfactants, PEG and vitamin E-TPGS. Please see claims 18-26; [0094], [0101].

Broder et al. and McChesney-Harris do not disclose the claimed solubility of the taxane compound at room temperature. However, the Examiner refers to Goodman & Gilman's, which teaches that paclitaxel has very limited solubility and must be administered in a vehicle of 50% ethanol and 50% polyethoxylated castor (CREMOPHOR EL™). Please see page 1260, second column, the paragraph under Figure 51-13.

Therefore, in view of Goodman & Gilman's teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the oral compositions used in the methods of Broder et al. and McChesney-Harris such that the taxane has sufficient solubility necessary to render the oral composition therapeutically effective. Absent evidence to the contrary, such a modification would have been motivated by the reasonable expectation of producing an oral composition which when orally administered is readily bioavailable.

Concerning the claims drawn to preferred inhibitory doses of taxane (ID_{50}), it would have been obvious to one of ordinary skill in the art at the time the invention was

made to further modify the methods of Broder et al. and McChesney-Harris such that the taxane is administered at a dose, which is effective to exhibit clinical and thus therapeutic activity against the taxane-responsive cancers. This is further evidenced by Goodman & Gilman's, which discloses that cell toxicity is dependent upon drug concentration as well as duration of cell exposure. With respect to the use of saline as a diluent, this would have been obvious to one of ordinary skill in the art since saline is a conventional diluent in the pharmaceutical art.

Finally, the Examiner notes that claim 1 contains "consisting essentially of" language. However, "a consisting essentially of'" claim occupies a middle ground between closed claims that are written in a "consisting of" format and fully open claims that are drafted in a "comprising" format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). See also Atlas Powder v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); In re Janakirama-Rao, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); Water Technologies Corp. vs. Calco, Ltd., 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355. Please see MPEP 2111.03.

Conclusion

Claims 1-17 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is 571-272-0572. The examiner can normally be reached on Mon-Fri from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached at 571-272-0584. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

CDM

March 20, 2004

Cybille Delacroix-Muirheid
Patent Examiner Group 1600